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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,896	08/31/2001	Kevin P. Baker	P2548P1C19	5992

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,896	BAKER ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-35 and 38-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *32-34* is/are allowed.

6)☒ Claim(s) *22-31,35 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 22-35 and 38-41 are pending in the instant application. Claims 22-26 and 35 have been amended and claims 36 and 37 have been canceled as requested by Applicant in Paper Number 11, filed June 26, 2003.

All claims are currently under examination.

Withdrawn Objections and Rejections

2. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Objection to Specification

3. The objections to the specification are withdrawn in view of Applicants' amendment.

Response to Amendment

4. The declaration under 37 CFR 1.132 filed June 26, 2003 is sufficient to overcome the rejection of claims 22-41 based upon lack of utility under 35 U.S.C. § 101.

Claim Objections

5. Claims 22-31 and 35 are objected to because of the following informalities:

5.1 Claims 27-31 and 35 are objected to because in subparts (a-d) of claims 27 and 35 and in claims 28-31, because the phrase "a nucleic acid sequence ***of*** the polypeptide shown in Figure 20

(SEQ ID NO: 50)". The examiner is interpreting that Applicants intend that the phrase should be "a nucleic acid sequence ***encoding*** the polypeptide shown in Figure 20 (SEQ ID NO: 50)".

5.2 Claims 22-27 and 35 are also objected to because in subpart (d) of the claims, "lacking ***it*** associated" should be "lacking ***its*** associated" to be grammatically correct.

Appropriate correction is required.

Priority Determination

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

6. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Since the instant application has utility and is enabled for use as a diagnostic for a tumor in a tissue, and this use was disclosed in provisional application 60/113, 296, filed Dec. 22, 1998, the instant application is considered to have an effective date of that provisional. The instant application also claims benefit of provisional 60/069,702, filed Dec. 16, 1997 though PCT/US98/25108, filed Dec. 1, 1998. However, those two applications do not disclose that the nucleic acids can be used as a diagnostic for a tumor in a tissue, and therefore do not meet the utility requirements and the requirements of 35 U.S.C. § 112, first paragraph. Therefore, those prior applications do not meet

those requirements and, therefore, are unavailable under 35 U.S.C. § 120 or § 119(e). The effective priority date of the instant application is considered to be the filing date of provisional 60/113, 296, Dec. 22, 1998.

New Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 22-27, 31, 35 and 38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Holtzman et al., US Patent Application Publication US20020028508, effective filing date, April 23, 1998 (09/065,661).

Claims 22-27, 31, 35 and 38-41 encompass nucleic acid molecules encoding a polypeptide having at least 80%, 85%, 90% or 95% sequence identity to the polypeptide of SEQ ID NO: 50, or 99% or 100% identity to the amino acid sequence of the extracellular domain of SEQ ID NO: 50 lacking its associated signal peptide, or that hybridizes under high stringency conditions to the nucleic acid sequence of SEQ ID NO: 49, vectors comprising the nucleic acids and expression vectors wherein the nucleic acid is operably linked to control sequences recognized by a host cell transformed by the vector, and host cells comprising the vectors, wherein said host cell is a CHO cell, an *E.coli* or a yeast cell.

Holtzman et al. disclose a nucleic acid sequence (SEQ ID NO: 1) that is 94.1% identical to the nucleic acid molecule of SEQ ID NO: 49 of the instant invention, and having a local similarity of 98% identity, and that encodes a protein (SEQ ID NO: 2) that is 96.8% identical to the protein of SEQ ID NO: 50 of the instant invention (see attached sequence alignments). The instant application identifies the signal sequence as amino acids 1-26 and the extracellular domain as amino acids 27-109 of SEQ ID NO: 50, the extracellular domain. The protein of Holtzman is identical to the extracellular domain, amino acids 27-109, of SEQ ID NO: 50. The nucleic acid of Holtzman et al. would also hybridize under high stringency conditions to the nucleic acid of SEQ ID NO: 49 of the instant application. Holtzman et al. also teach vectors and expression vectors (paragraph 0246), and host cells, wherein said host cell can be a CHO cell, an *E.coli* or a yeast cell (paragraph 0258). Therefore, Holtzman et al. anticipates the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 22-27, 31, 35 and 38-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-27, 31, 35 and 38-41 are indefinite because claims 22-27, 31 and 35 encompass nucleic acids encoding a polypeptide comprising the extracellular domain of the protein of SEQ ID NO: 50 lacking its signal sequence. The recitation of "the extracellular domain"...."lacking its associated signal sequence" (claim 22, part (d), for example) is

indefinite, as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. The other claims are rejected for depending from claim 22.

Maintained rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9.1 Claims 22-31, 35 and 38-41 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 49, or fragments of the nucleic acid sequence, does not reasonably provide enablement for polynucleotides encoding the protein of SEQ ID NO: 50 or encoding proteins at least 80%, 85%, 90%, 95%, or 99% to the protein of SEQ ID NO: 50. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants have overcome the utility rejection, and Applicants have demonstrated that the nucleic acids can be used as a diagnostic for a tumor in a tissue, because they are amplified in certain tumors. However, claims 22-31, 35 and 38-41 encompass nucleic acids encoding polypeptides, and because of the degenerency of the genetic code, such nucleic acids could deviate significantly from the nucleic acid of SEQ ID NO: 49. Additionally, nucleic acids encoding polypeptides having at least 80%, 85%, 90%, 95%, or 99% to the protein of SEQ ID

NO: 50, would deviate even more so from the nucleic acid of SEQ ID NO: 49. Because of this, such nucleic acids would not be useful as diagnostic markers. Applicants have amended the claims to recite the limitation "wherein said polypeptide is overexpressed in lung and colon tumors", and on pages14-15 assert that such variant and fragment polypeptides would have the same diagnostic utility as the wild-type PRO347 polypeptide, in that such variant and fragments of PRO347 would have the same or at least similar utility to full length polypeptides in detecting, monitoring or preparing treatments for various cancers. Applicants also cite *in re Wands* and assert that a considerable amount of experimentation is permissible, if it is routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants' arguments have been fully considered but are not deemed persuasive. The data in the specification (and reviewed in the declaration) show that gene copy number is increased in certain tumor tissue samples. However, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression. For example, Pennica et al. (1998, PNAS USA 95:14717-14722; Exhibit A of the declaration) disclose that,

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left-hand column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". Furthermore, an increase in mRNA

expression does not necessarily result in increased protein expression. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript) p. 1863, second paragraph, and Figure 1).

Therefore, it is not predictable that the PRO347 polypeptide is overexpressed in any tumor cell in which the encoding nucleic acid is amplified, and the rejection is maintained.

9.2 Claims 22-26, 35 and 38-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in the previous Office Action, Paper No. 10, at pages 6-8, and below.

Applicants traverse the rejection and have amended the claims to recite the limitation "wherein said polypeptide is overexpressed in lung and colon tumors", and assert on pages 15-18 of the response that as amended, the claims satisfy the written description requirement. Applicants submits that the present application discloses a combination of the elements required for an adequate written description (page 16, second paragraph of the response), and that the claims have been amended such that the claimed variant and fragment nucleic acids are required to have a sufficient sequence identity with the wild type nucleic acid sequence encoding PRO347, in addition to encoding a polypeptide that is overexpressed in lung and colon tumors.

Applicants' arguments have been fully considered but are not deemed persuasive. As discussed above, amplification of a nucleic acid does not necessarily result in an increase of the encoded polypeptide, and therefore the functional recitation is not considered adequate to overcome the written description requirement, and the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 35 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended the claim to Claim recite the limitation "under high stringency conditions". However, on page 30 of the specification, there are several different hybridization conditions exemplified by high stringency conditions, so that the metes and bounds of the patent protection desired are not clearly set forth. This rejection would be overcome by reciting one of the hybridization conditions recited in the specification, such as the one recited on page 18 of the response, as well as the high-stringency wash conditions.

It is believed that all pertinent arguments have been answered.

Conclusion

11.1 Claims 32-34 are allowed.

11.2 Claims 22-31, 35 and 38-41 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

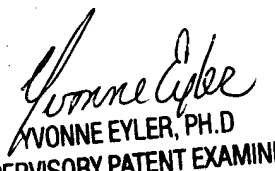
Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



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